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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,991	03/15/2006	Laurent Francois Andre Hennequin	09963.0008	5523

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EXAMINER	
WILLIS, DOUGLAS M	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
05/26/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/571,991	HENNEQUIN ET AL.	
	Examiner	Art Unit	
	DOUGLAS M. WILLIS	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03-15-06; 07-11-06; 01-09-07; 07-14-08; 12-11-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

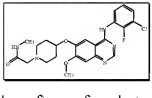
DETAILED ACTION

Status of the Claims / Priority

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the *Final Rejection*, mailed on January 6, 2009, has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission, filed on April 6, 2009, has been entered.

Claims 38-43 are pending in the current application. According to the *Amendments to the Claims*, filed April 6, 2009, claims 39, 40, 42 and 43 were amended and claims 1-37 and 44-71 were cancelled. This application is a 35 U.S.C. § 371 National Stage Filing of International Application No. PCT/GB2004/03937, filed September 15, 2004, which claims priority under 35 U.S.C. § 119(a-d) to: a) EP 03292309.6.7, filed September 19, 2003; and b) EP 04291248.5, filed May 14, 2004.

Status of Restrictions / Election of Species

Applicant's affirmation of the following election, with traverse, in the reply filed on  December 11, 2008, is acknowledged: a) Group I, claims 38-43; and b) substituted quinazolinamine - p. 58, example 1, shown left, and hereafter referred to as 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(*N*-methylcarbamoyl-methyl)piperidin-4-yl]oxy}quinazoline.

The requirement was made FINAL in the *Final Rejection*, mailed on January 6, 2009.

The sections of U.S.C. Title 35 that formed the basis of prior rejections formulated, as well as any references supporting said rejections, that are not included with this Office action, may be found in the *Non-Final Rejection*, mailed on August 19, 2008, or the *Final Rejection*, mailed on January 6, 2009. Furthermore, any rejections or objections of record not explicitly addressed herein below, are hereby withdrawn, in light of applicant's arguments and/or the *Amendments to the Claims*, filed April 6, 2009.

Thus, a third Office action and prosecution on the merits of claims 38-43 is contained within.

New Specification Objection

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase *Not Applicable* should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art (including information disclosed under 37 CFR 1.97

and 1.98).
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825).

Applicant is advised to format the specification according to 37 CFR 1.77(b) above. Revisions should particularly include and/or address: a) bold-type, underline and upper case formatting; and b) sections (b-i), where applicable. Appropriate correction is required.

New Specification Objection - Title

Applicant is reminded of the proper content of the title of the invention.

The title of the invention should be brief, but technically accurate and descriptive, preferably from two to seven words. See 37 CFR 1.72(a) and MPEP § 606.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. In the revised title, the examiner suggests including: a) 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(*N*-methylcarbamoylmethyl)piperidin-4-yl]oxy}quinazoline; and b) the alleged utility possessed by 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(*N*-methylcarbamoylmethyl)piperidin-4-yl]oxy}quinazoline.

New Claim Objections

Claims 38 and 41 are independently objected to because of the following informalities: *and its pharmaceutically acceptable salts* should be replaced with *or its pharmaceutically acceptable salts*. Appropriate correction is required.

New Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

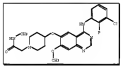
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

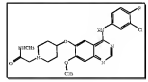
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 38-43 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Himmelsbach, et al. in US 6,924,285.

The instant application recites a compound chosen from 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(*N*-methylcarbamoylmethyl)piperidin-4-yl]oxy}quinazoline, shown to the left, or a pharmaceutically acceptable salt or pharmaceutical composition thereof, which possesses anti-tumor activity.



Himmelsbach, et al. (US 6,924,285), as cited on the IDS, teaches a compound chosen from 2-(4-(4-(3-chloro-4-fluorophenylamino)-7-methoxyquinazolin-6-yloxy)piperidin-1-yl)-*N*-methylacetamide, shown to the right, or a physiologically acceptable salt or pharmaceutical composition thereof, as therapeutic agents for treating tumoral diseases [columns 69 and 70, compound 38; physiologically acceptable salts - column 18, lines 41-48; and pharmaceutical compositions - column 1, lines 17-18 and claims 8



and 9].

The only difference between the instantly recited 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(*N*-methyl-carbamoylmethyl)piperidin-4-yl]oxy}quinazoline and Himmelsbach's 2-(4-(4-(3-chloro-4-fluorophenylamino)-7-methoxyquinazolin-6-yloxy)piperidin-1-yl)-*N*-methylacetamide is the instantly recited 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(*N*-methylcarbamoylmethyl)piperidin-4-yl]oxy}quinazoline has a -F attached to C-2 of the phenyl ring, whereas Himmelsbach's 2-(4-(4-(3-chloro-4-fluorophenylamino)-7-methoxyquinazolin-6-yloxy)piperidin-1-yl)-*N*-methylacetamide has a -F attached to C-4 of the phenyl ring.

MPEP § 2144.09 states *compounds which are position isomers, having the same radicals in physically different positions on the same nucleus, are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties.* {See *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977)}.

Similarly, the courts have recognized that *there is little difference between the ortho- and para- positions occupied by* -F *in the substituted quinazolines and pharmaceutical compositions above, as similar circumstances have arisen many times. As a matter of fact, it is well established that position isomers are structurally prima facie obvious, even in the absence of a teaching to modify. The isomers are expected to have the same method of preparation and generally the same properties. It is this expectation that is deemed the motivation for preparing such isomers.* (See *Ex parte Englehardt,* 208 USPQ 343, 349; *In re Mehta,* 146 USPQ 284, 287; *In re Surrey*, 138 USPQ 67; *Ex Parte Ullyot,* 103 USPQ 185; *In re Norris,* 84 USPQ 459; *Ex. Parte Naito,* 168 USPQ 437, 439; *Ex parte Allais,* 152 USPQ 66; *In re Wilder,* 166 USPQ 545, 548; *Ex parte Henkel,* 130 USPQ 474; *Ex parte Biel,* 124 USPQ 109; *In re Petrzilka,* 165 USPQ

327; *In re Crownse,* 150 USPQ 554; *In re Fouche,* 169 USPQ 431; *Ex parte Ruddy,* 121 USPQ 427; *In re Wiechert,* 152 USPQ 249, *In re Shetty,* 195 USPQ 753; and *In re Jones,* 74 USPQ 152, 154).

Moreover, *position isomerism has been used as a tool to obtain new and useful drugs* (see *Ex parte Englehardt*) and... *is fact of close structural similarity* (see *In re Mehta*). Similarly, *a novel useful chemical compound, which is homologous or isomeric with compounds of the prior art, is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds.* (See *In re Schechter and LaForge,* 98 USPQ 144, 150). *Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds... and a known compound may suggest it's analog or isomers, either geometric (cis v. trans) or positional isomers (e.g. ortho v. para).* (See *In re Deuel* 34 USPQ2d 1210, 1214).

Thus, since: a) Himmelsbach teaches 2-(4-(4-(3-chloro-4-fluorophenylamino)-7-meth-oxyquinazolin-6-yloxy)piperidin-1-yl)-*N*-methylacetamide, where -F is attached to C-4 of the phenyl ring; b) MPEP § 2144.09 states that *positional isomers are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties*; and c) the courts have recognized that *positional isomers are structurally* prima facie *obvious and are expected to have the same method of preparation*, one having ordinary skill in the art, at the time this invention was made, would have been motivated to utilize the teachings of Himmelsbach and formulate a positional isomer, pharmaceutically acceptable salt or pharmaceutical composition of Himmelsbach's 2-(4-(4-(3-chloro-4-fluorophenylamino)-7-meth-oxyquinazolin-6-yloxy)piperidin-1-yl)-*N*-methylacetamide, where -F is attached to C-2 of the

phenyl ring, with a reasonable expectation of success and similar therapeutic activity, rendering claims 38-43 obvious.

Finally, although not explicitly discussed herein, applicant is advised to note that the Himmelscach reference contains additional species that may obviate 4-(3-chloro-2-fluoro-anilino)-7-methoxy-6-{[1-(*N*-methylcarbamoylmethyl)piperidin-4-yl]oxy}quinazoline. Consequently, any amendments to the claims to overcome rejections rendered under 35 U.S.C. § 103(a) should address this reference as a whole and should not be limited to the species discussed or disclosed explicitly herein.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

New Claim Rejections - Obviousness-type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute), so as to prevent the unjustified or improper timewise extension of the *right to exclude* granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claims because the examined application claim

is either anticipated by, or would have been obvious over, the reference claims. {See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969)}.

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 38-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24-35 of copending Application No. 12/147,250. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 24-35 in the copending application recites definitions for G^1, G^2, X^1, X^2, R^1 and Q^1which provide overlapping subject matter with respect to the instant claims. For example, if R^1 is -CH_3 and Q^1 is piperidin-4-yl, optionally substituted with -$CH_2C(O)NHCH_3$ [*N*-(1-6C)alkylcarbamoyl(1-6C)alkyl], in claim 33 of the copending application, then the recited species of the copending application is identical to the species recited in the instant application, *4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoylmethyl)piperidin-4-yl]oxy}-*

quinazoline.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DOUGLAS M. WILLIS, whose telephone number is 571-270-5757. The examiner can normally be reached on Monday thru Thursday from 8:00-6:00 EST. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DOUGLAS M WILLIS/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, AU 1624